REMARKS

Applicants herein cancels claims 1-8, without prejudice and reserving the right to file one or more divisional patent application(s) directed to the subject matter therein, and adds new claims 9-24. Support for these claims is found within the specification. For example,

the specification discloses that the measure of polyamine content in the sample is at least one of polyamine content in the sample; aldehyde compound content formed from the polyamine in the sample; polyamine oxidase activity in the sample; and protein content of polyamine oxidase in the sample. [Claims 9, 16, 17, and 24; see Specification, para. [0017]];

the specification discloses that biological samples for measurement are taken from subjects, and that these biological samples include blood plasma, urine, saliva, cerebrospinal fluid and bone marrow fluid. [Claims 10 and 18; see Specification, para. [0018]]; and

the specification discloses that known biogenic polyamines may include, but are not limited to, putrescine, cadaverine, spermidine, spermine, 1,3-diaminopropane, caldine, homospermidine, 3-aminopropylcadaverine, norspermine, thermospermine, caldopentamine, and so on. [Claims 14, 15, 22, and 23; see Specification, para. 0019]];

the specification discloses that polyamines are metabolized by oxidation, acetylation, transamination and carbamoylation, and polyamine oxidase is the enzyme that involves in the oxidation of polyamine, and polyamine receives oxidative deamination by polyamine oxidase, thereby aldehyde compounds such as acrolein would be produced [Claims 11, 12, 13, 19, 20, and 21; see Specification, para. [0020]].

the specification discloses that (i) acrolein content, polyamine content, or polyamine oxidase activity of the cerebral infarction patients in plasma was higher than healthy subjects, (ii) stroke/asymptomatic cerebral infarction could be diagnosed using these measured values as an indicator, and (iii) that the patients of stroke/asymptomatic cerebral infarction can be screened using the measured values as an indicator and based on those values, it would be possible to diagnose that those subjects showing higher values may be suffering from stroke/asymptomatic cerebral infarction with high probability. [Claims 9, 17; see Specification, para. [0029]];

The Examiner found that the benefit of priority is to March 25, 2004.

The Examiner contended that acrolein also is known as 2-propenal, which is spontaneously formed from 3-aminopropanal during the oxidation of polyamine (citing Sakata, 2003).

OBJECTIONS

Title

The Examiner contended that the title of the invention is not descriptive and required a new title that is clearly indicative of the invention to which the claims are directed. Applicants appreciate the Examiner's suggested title "Method of diagnosing apoplectic stroke/asymptomatic brain infarction using acrolein content" and proffer that title as the replacement title Applicants therefore respectfully request withdrawal of this ground for objection.

Drawings

The Examiner objected to the drawings on the ground that Figures 3 and 4 are not clear/recognizable, and required corrected drawing sheets in compliance with 37 CFR 1.121(d). Applicants herein submit replacement drawing sheets containing Figures 3 and 4. Applicant respectfully requests withdrawal of the instant objection.

REJECTIONS

35 U.S.C. § 112, first paragraph

Claims 1 and 4: Aldehydes

Claims 1 and 4 have been rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the specification does not reasonably provide enablement for any and all aldehyde compounds, and does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The Examiner conceded that the application is enabling for an aldehyde compound that is acrolein.

The Examiner contended (i) that the art of biotechnology is a highly unpredictable art; (ii) that it would be an undue burden for one of ordinary skill in the art to test any and all aldehyde compounds to see if they can be used as diagnosing marker for stroke/asymptomatic cerebral infarction; and (iii) that there is no prior art known to the Examiner that establishes that

one of ordinary skill in the art would have known at the time the invention was made that all or any aldehyde compound can be used as a diagnosing marker for stroke/asymptomatic cerebral infarction.

The Examiner further contended that Applicants only have shown acrolein content in plasma of patients with brain disorder, citing Example 1, page 9, of the specification. The Examiner contended that with only knowing the result of aldehyde compound produces acrolein, such broad claims are not enabled by the instant specification when one of ordinary skill in the art is only given one particular aldehyde compound-acrolein that function as diagnosing marker for stroke/asymptomatic cerebral infarction.

The Examiner contended that because the state of the art is that there is no art, one of ordinary skill in the art would have no way of knowing if all or any of the aldehyde compounds can be used as diagnosing marker for stroke/asymptomatic cerebral infarction without any reference to all aldehyde compounds that function as diagnosing marker for stroke/asymptomatic cerebral infarction.

Applicants' Response

Applicants have cancelled claims 1 and 4 rendering this ground for rejection moot as to those claims. Applicants herein proffer new independent claim 9, and new independent claim 17 which replace cancelled claims 1 and 4, respectively.

With regard to the Examiner's comments to the extent that they apply to new claims 9 and 17, Applicants respectfully urge that:

First, the Federal Circuit has expressly rejected the contention that claims of a patent must be construed as being limited to the embodiments. See Liebel-Flarsheim, Co. v. Medrad, Inc., 358 F.3d 898, 906 (Fed. Cir. 2004) (citing ACTV, Inc. v. Walt Disney Co., 346 F.3d 1082, 1091 (Fed. Cir. 2003); Apex, Inc. v. Raritan Computer, Inc., 325 F.3d 1364, 1377 (Fed. Cir. 2003), Altiris, Inc. v. Symantec Corp., 318 F.3d 1363, 1373 (Fed. Cir. 2003), Tex. Digital Sys., Inc. v. Telegenix, Inc., 308 F.3d 1193, 1204-05 (Fed. Cir. 2002); Teleflex, Inc. v. Ficosa N. Am. Corp., 299 F.3d 1313, 1327 (Fed. Cir. 2004)); and SRI Int'l v. Matsuchita Elec. Corp. of Am., 775 F.2d 1107, 1121 n. 14 (Fed. Cir. 1985) (en banc)). Here, acrolein is disclosed expressly as the best mode. The sole purpose of the best mode requirement "is to restrain inventors from

applying for patents while at the same time concealing from the public preferred embodiments of their inventions which they have in fact conceived." In re Glass, 492 F.2d 1228, 122 (CCPA 1974). By disclosing acrolein and plasma as the best mode, Applicants therefore have disclosed that at the time the inventors filed their patent application, this mode of practicing the claimed invention was considered by the inventors to be better than any other. That does not mean it is the only mode of practicing the invention. Indeed, the specification discloses (1) that known biogenic polyamines may include, but are not limited to, putrescine, cadaverine, spermidine, spermine, 1,3-diaminopropane, caldine, homospermidine, 3-aminopropylcadaverine, norspermine, thermospermine, caldopentamine, and so on. [see Specification, para. 0019], and (2) that the measure of polyamine content in the sample is at least one of polyamine content in the sample; aldehyde compound content formed from the polyamine in the sample; polyamine oxidase activity in the sample; and protein content of polyamine oxidase in the sample. [see Specification, para. [0017]].

Second, the Federal Circuit has held that claims should not be narrowed to the preferred embodiments unless the specification suggested the inventor intended such narrow coverage. Id. ("even when the specification describes only a single embodiment, the claims of the patent will not be read restrictively unless the patentee has demonstrated clear intention to limit the claim scope using 'words or expressions of manifest exclusion or restriction'"); see also Lizardtech, Inc. v. Earth Resource Mapping, Inc., 433 F.3d 1373, 1377 (Fed. Cir. 2006) (citing JVW Enterprises, Inc. v. Interact Accessories, Inc., 424 F.3d 1324, 1335 (Fed. Cir. 2005) and Phillips v. AWH Corp., 415 F.3d 1303, 1323 (Fed. Cir. 2005) (en banc)). Here, inventor expressly states that the present invention is not limited to the best mode. In para. [0017], the specification discloses different measures of polyamine content. In para. [0019], the specification discloses biogenic polyamines. In para. [0020], the specification expressly states that the preferred aldehyde compound in the present invention may be acrolein, but is not so limited by it. Therefore, because the specification does not contain "words or expressions of manifest exclusion or restriction" that would demonstrate a clear intention to limit claim scope to only acrolein, a person of ordinary skill in the art who reads the instant specification would reasonably know that the language of the specification indicates that any measure of polyamine content of any biological sample can be used.

Third, the scope of enablement is that which is described in the specification plus the scope of what would be known to a person of ordinary skill in the art without undue experimentation. See, e.g., Invitrogen Corp. v. Clontech Labs, Inc., 429 F.3d 1052, 1070-71 (Fed. Cir. 2005). The specification provides a skilled artisan with detailed guidance as to how to make and use the claimed invention, and the properties of polyamines as a class of compounds are known to those of ordinary skill in the relevant art. Applicant therefore respectfully urges that a skilled artisan in this field would be able to read the specification and follow the guidance of the exemplified embodiment to make and use a measure of polyamine content as claimed. This may require some routine experimentation, but routine experimentation is not undue experimentation.

MPEP 2164.02 provides that for the claimed genus of measures of polyamine content, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be used in that manner without undue experimentation. Furthermore, Applicants respectfully urge that compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, does not turn on whether an example for every biological sample, or every measure of the content of a biogenic polyamine is disclosed.

Since the instant specification provides a person of ordinary skill in the art with sufficient enablement so that such a person can practice the invention commensurate in scope with the claims as amended, Applicants respectfully request that this ground for rejection be withdrawn.

Claims 1 and 4: Biological Samples

Claims 1 and 4 have been rejected under 35 U.S.C. § 112, first paragraph on the ground that the specification does not reasonably provide enablement for any and all biological samples because not all/any biological sample has polyamine and the enzyme that converts polyamine to aldehyde compound for measurement, and does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to practice the invention commensurate in scope with these claims. The Examiner acknowledged that claims 1 and 4 are enabled for plasma as a biological sample.

The Examiner contended (i) that the art of biotechnology is a highly unpredictable art; (ii) that it would be an undue burden for one of ordinary skill in the art to test any and all biological sample to see if they can be used to measure aldehyde compound; and (iii) that there is no prior art known to the Examiner that establishes that one of ordinary skill in the art would have known at the time the invention was made that all or any biological sample can be used to measure aldehyde compound to diagnose stroke/asymptomatic cerebral infarction.

The Examiner further contended that Applicant only has shown plasma as biological sample, citing Examples 1-4, starting at page 9, of the specification. The Examiner contended that with only knowing the result of plasma as biological sample, such broad claims are not enabled by the instant specification when one of ordinary skill in the art is only given one particular biological sample (plasma) for measurement for the diagnose of stroke/asymptomatic cerebral infarction.

The Examiner contended that because the state of the art is that there is no art, one of ordinary skill in the art would have no way of knowing if all or any biological sample can be used to measure aldehyde compound content to diagnose stroke/asymptomatic cerebral infarction because not all biological sample contain polyamine and the enzyme that convert polyamine to aldehyde compound without any reference to all biological sample for aldehyde compound measurement to function as diagnosing marker for stroke/asymptomatic cerebral infarction.

In short, the Examiner contended the claims are unduly broad and do not find proper support from the instant specification.

Applicants' Response

Applicants have cancelled claims 1 and 4 rendering this ground for rejection moot. Applicants herein proffer new independent claim 9, and new independent claim 17 which replace cancelled claims 1 and 4, respectively.

With regard to the Examiner's comments to the extent that they apply to new claims 9 and 17, Applicants respectfully urge that:

First, the Federal Circuit has expressly rejected the contention that claims of a patent must be construed as being limited to the embodiments. See Liebel-Flarsheim, Co. v. Medrad, Inc., 358 F.3d 898, 906 (Fed. Cir. 2004) (citing ACTV, Inc. v. Walt Disney Co., 346 F.3d 1082,

1091 (Fed. Cir. 2003); Apex. Inc. v. Raritan Computer, Inc., 325 F.3d 1364, 1377 (Fed. Cir. 2003), Altiris, Inc. v. Symantec Corp., 318 F.3d 1363, 1373 (Fed. Cir. 2003), Tex. Digital Sys., Inc. v. Telegenix, Inc., 308 F.3d 1193, 1204-05 (Fed. Cir. 2002); Teleflex, Inc. v. Ficosa N. Am. Corp., 299 F.3d 1313, 1327 (Fed. Cir. 2004)); and SRI Int'l v. Matsuchita Elec. Corp. of Am., 775 F.2d 1107, 1121 n. 14 (Fed. Cir. 1985) (en banc)). Here, blood plasma is disclosed expressly as the best mode. The sole purpose of the best mode requirement "is to restrain inventors from applying for patents while at the same time concealing from the public preferred embodiments of their inventions which they have in fact conceived." In re Glass, 492 F.2d 1228, 122 (CCPA 1974). By disclosing blood plasma as the best mode, the applicants therefore have disclosed that at the time the inventors filed their patent application, this mode of practicing the claimed invention was considered by the inventors to be better than any other. That does not mean it is the only mode of practicing the invention.

Second, the Federal Circuit has held that claims should not be narrowed to the preferred embodiments unless the specification suggested the inventor intended such narrow coverage. Id. ("even when the specification describes only a single embodiment, the claims of the patent will not be read restrictively unless the patentee has demonstrated clear intention to limit the claim scope using 'words or expressions of manifest exclusion or restriction'"); see also Lizardtech, Inc. v. Earth Resource Mapping, Inc., 433 F.3d 1373, 1377 (Fed. Cir. 2006) (citing JVW Enterprises, Inc. v. Interact Accessories, Inc., 424 F.3d 1324, 1335 (Fed. Cir. 2005) and Phillips v. AWH Corp., 415 F.3d 1303, 1323 (Fed. Cir. 2005) (en banc)). Here, the inventors expressly state that the present invention is not limited to the best mode. Indeed, in para. [0018], the specification expressly discloses that the biological sample for measurement is at least one selected from blood plasma, urine, saliva, cerebrospinal fluid, and bone marrow fluid. Because the specification does not contain "words or expressions of manifest exclusion or restriction" that would demonstrate a clear intention to limit claim scope to only acrolein or only plasma, a person of ordinary skill in the art who reads the instant specification would reasonably know that the language of the specification indicates that any measure of polyamine content of any biological sample can be used.

Third, the scope of enablement is that which is described in the specification plus the scope of what would be known to a person of ordinary skill in the art without undue

experimentation. See, e.g., Invitrogen Corp. v. Clontech Labs, Inc., 429 F.3d 1052, 1070-71 (Fed. Cir. 2005). The specification provides a skilled artisan with detailed guidance as to how to make and use the claimed invention. The properties of the disclosed biological samples are known to those of ordinary skill in the relevant art. Applicants urge that a skilled artisan in this field therefore would be able to read the specification and follow the guidance of the exemplified embodiments to make and use a given biological sample as claimed. This may require some routine experimentation, but routine experimentation is not undue experimentation.

Applicants further urge that MPEP 2164.02 provides that for the claimed genus of measures of polyamine content, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be used in that manner without undue experimentation. Furthermore, Applicants respectfully urge that compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, does not turn on whether an example for every biological sample is disclosed.

Since the instant specification provides a person of ordinary skill in the art with sufficient enablement so that such a person can practice the invention commensurate in scope with the claims as amended, Applicants respectfully request that this ground for rejection be withdrawn..

35 U.S.C. § 112, second paragraph

Claims 1, 3, 4, and 6 have been rejected under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps.

The Examiner contended that Claims 1 and 4 are incomplete because each lacks information about how the sampling/measuring/diagnosing is accomplished; especially a correlating step to accomplish the preamble is missing as how the diagnosis/screening is made (what is the control? how the measured value is compared and used in the diagnosis? etc.).

Applicants have canceled claims 1, 3, 4, and 6, rendering this ground for rejection moot.

Claim 4 also has been rejected because the method is screening for a patient, however, the Examiner contended that the sample is taken from a subject. Applicants have canceled claim 4 rendering this ground for rejection moot.

35 U.S.C. § 103(a)

Claims 1, 3, 4, and 6 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of Els (2001, IDS submitted 2/8/2010) ("Els"), Ivanova (1998) ("Ivanova"), and Sakata (2003, IDS submitted 2/8/2010) ("Sakata").

Els

The Examiner contended that Els teaches a diagnostic method for stroke comprising: sampling a biological sample from a subject by using blood samples from patients (citing page 43, right column, 1st full paragraph), measuring polyamine in the sample (citing page 44, left column, 3rd paragraph), and diagnosing/screening stroke by correlating the polyamine/ spermidine level with clinical outcome and infarct volume (citing page 45, left column, 1st full paragraph and Figure 2, part of Claims 1 and 4). The Examiner acknowledged that Els does not teach that the aldehyde compound measured is acrolein.

Ivanova

The Examiner contended that Ivanova teaches the oxidation of polyamine that generates 3-aminopropanal during the onset of cerebral ischemia (citing page 330, right column, end of 1st full paragraph).

Sakata

The Examiner contended that Sakata teach the spontaneous formation of acrolein (claims 3 and 6) from 3-aminopropanal: product of the oxidation of polyamine (citing page 371, left column 1st and 2nd paragraphs).

The Examiner contended that it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Els by measuring acrolein as aldehyde compound (Claims 1, 3, 4, and 6) in samples from subjects to diagnose/screen for stroke/asymptomatic cerebral infarction because (1) Els teaches that polyamine can be used as diagnose marker for stroke, (2) Ivanova teaches the oxidation of polyamine to produce 3-

aminopropanal during onset of cerebral ischemia, and (3) Sakata teaches the spontaneous formation of acrolein from 3-aminopropanal. The Examiner contended that one would have been motivated to make the modification because Els specifically described the correlation of polyamine/spermidine level with clinical outcome and infarct volume (citing page 45, left column, 1st full paragraph, and Figure 2), and Sakata teaches the spontaneous formation of acrolein from 3-aminopropanal: product of the oxidation of polyamine (during onset of cerebral ischemia as taught by Ivanova), and would reasonably have expected success in view of both Ivanova and Sakata's teachings.

Applicants' Response

Applicants have canceled claims 1, 3, 4, and 6, and proffer new independent claim 9, and new independent claim 17 which replace cancelled independent claims 1 and 4, respectively. Applicants therefore have addressed the Examiner's comments to the extent that they apply to new claims 9 and 17.

The instant specification discloses that

(1) asymptomatic brain infarction is mostly detected accidentally by diagnostic imaging,

(2) there have been no diagnostic markers available in blood or urine examination, and

(3) a simple and accurate diagnostic method is highly desirable. The present invention describes such a method.

For this reason, and the reasons below, Applicants urge (i) that at the time the invention was made, the claimed invention as a whole would not have been obvious to a person of ordinary skill in the art and (ii) that there is no plausible reason that would have prompted a person of ordinary skill in the art to combine the cited elements as suggested by the Examiner.

Failure to Disclose Every Element of the Claims

First, neither Els, Ivanova, nor Sakova, either alone or in combination, discloses, either expressly or inherently, every element of the claims. Applicants respectfully urge that the cited references, either taken alone or in combination, fail to teach or suggest either a diagnostic

method for asymptomatic cerebral infarction, comprising: (a) obtaining at least one biological sample from a subject; (b) measuring biogenic polyamine content in the biological sample; wherein a measure of biogenic polyamine content is at least two measures selected from a measure of polyamine content in the biological sample; a measure of aldehyde compound content formed from the polyamine in the biological sample; a measure of polyamine oxidase activity in the biological sample; and a measure of polyamine oxidase protein content in the biological sample; and (c) comparing the biogenic polyamine content of the biological sample in (b) to polyamine content of a biological sample of a healthy subject, wherein a difference in measured value of the subject in (a) compared to a measured value of a healthy subject or a subject suffering from brain disease other than stroke is indicative of an asymptomatic cerebral infarction as claimed in claim 9; or a screening method to identify a subject that has experienced an asymptomatic cerebral infarction, comprising: (a) obtaining at least one biological sample from the subject; (b) measuring biogenic polyamine content in the biological sample; wherein a measure of biogenic polyamine content is at least two measures selected from a measure of polyamine content in the biological sample; a measure of aldehyde compound content formed from the polyamine in the biological sample; a measure of polyamine oxidase activity in the biological sample; and a measure of polyamine oxidase protein content in the biological sample; and (c) comparing the difference between the measured biogenic polyamine content in (b) to a measured biogenic polyamine content of a healthy subject; wherein the difference in measured value in (c) is indicative of an asymptomatic cerebral infarction, as claimed in claim 17.

Els

As for Els, Applicants urge that Els fails to teach or suggest each and every element of the claims as amended. Applicants respectfully urge that Els discloses (1) that the level of polyamine was determined only in blood samples as a diagnostic measure; and (2) that all patients were symptomatic, i.e., they all have clinical signs of stroke/cerebral infarction. In contrast, the instant claims require at least two measures of biogenic polyamine content, and are directed to a diagnostic or screening method utilizing a measure of biogenic polyamine content in a biological sample for asymptomatic cerebral infarction. Applicants urge that a person of ordinary skill in the art would recognize that asymptomatic cerebral infarction and symptomatic acute focal cerebral ischemia, as disclosed by Els, are not equivalent. Indeed, the present

specification discloses that patients with asymptomatic cerebral infarction do not show any subjective symptoms (see specification, page 1, lines 21-22), while Els discloses (1) that all patients of their study showed an emboligenic territorial infarction, symptoms of which can include a loss of muscular control, diminution or loss of sensation or consciousness, or other symptoms. . Accordingly, Applicants respectfully urge that Els fails to teach or suggest every element of the instant claims.

Ivanova

The Examiner contended that Ivanova, teaches that the oxidation of polyamine that generates 3-aminopropanal during the onset of cerebral ischemia.

Applicants respectfully disagree and urge that Ivanova, like Els, fails to teach or suggest each and every element of the claims as amended, and when combined with Els, does not make up for the deficiencies of Els.

In response, Applicants respectfully urge that Ivanova discloses measuring polyamine oxidase activity in rats subjected to permanent occlusion of the middle cerebral artery. Applicants respectfully urge that a person of ordinary skill in the art would recognize that a subject of a permanent occlusion of the middle cerebral artery would experience symptoms including paralysis or weakness of the contralateral face and arm, and sensory loss. Accordingly, Applicants urge that these animals are symptomatic, and therefore are not an appropriate model for asymptomatic stroke. Therefore, the significance of polyamine metabolism remains uninvestigated as to asymptomatic stroke after Ivanova.

In contrast, Applicants urge that the instant claims are directed to a diagnostic or screening method for asymptomatic cerebral infarction utilizing a measure of biogenic polyamine content in a biological sample. Applicants urge that the instant specification teaches that asymptomatic cerebral infarction does not show any subjective symptoms (see specification, page 1, lines 21-22). Furthermore, Ivanova fails to teach or suggest at least the claim element of two measure of biogenic polyamine content. Indeed, as acknowledged by the Examiner, the state of the art at the time the invention was made is that there is no art.

Sakata

The Examiner contended that Sakata teach the spontaneous formation of acrolein from 3-aminopropanal: product of the oxidation of polyamine (citing page 371, left column 1st and 2nd paragraphs). Applicants herein address the Examiner's contention even though Applicants could not find the Examiner's citation since the Sakata reference consists of pages 143-149.

Applicants respectfully disagree and urge that Sakata, like Ivanova and Els, fails to teach or suggest each and every element of the claims as amended, and when combined with Els and Ivanova, does not make up for the deficiencies of either Els and/or Ivanova.

In response, Applicants urge that Sakata discloses the levels of polyamines, its oxidized product acrolein, and amine oxidase in plasma of patients with renal failure. Applicants urge that, renal failure is a different disease from asymptomatic cerebral infarction with different symptoms and different effects. Paragraph [0008] of the specification distinguishes renal failure from asymptomatic stroke and discloses that although it was known that acrolein generated by oxidative degradation of polyamine is involved in uremia in kidney diseases, there has not been sufficient knowledge on whether this mechanism is involved in other cerebrovascular disease, such as stroke. The instant claims are directed to a diagnostic or screening method utilizing a measure of biogenic polyamine content in a biological sample for asymptomatic cerebral infarction, not renal failure, and not symptomatic stroke.

No Plausible Reason to Combine the Cited References

Second, no basis in the art has been identified for combining or modifying the cited references, and the courts warn against employing hindsight reasoning using the invention as a roadmap to find its prior art components. Indeed, there is no plausible reason that would have prompted a person of ordinary skill in the art to combine the cited elements to reach the claimed invention as the Examiner suggests.

Generally, a motivation to combine prior art references generally may be found in the prior art explicitly or implicitly, in the prior art references themselves, in the knowledge of those of ordinary skill in the art, or from "the nature of the problem to be solved leading inventors to look to references relating to possible solutions to that problem" (Ruiz, 69 USPQ2d at 1690). However, there is nothing in Els, Ivanova, or Sakata to suggest a diagnostic or screening method

for asymptomatic cerebral infarction utilizing at least two measures of a biogenic polyamine from a biological sample.

No Reasonable Degree of Predictability of Success

The Examiner further contended that from the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention, and therefore the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary. Applicants respectfully disagree.

There is no reasonable degree of predictability of success in the proposed modification or combination. Indeed, a great deal of undue experimentation would have been necessary for a person of ordinary skill in the art to start from Els, Ivanova, and Sakata and result in the claimed invention. A person of ordinary skill has good reason to pursue the known options within his or her technical grasp "[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions." Here, although the relative skill in the art is high, the art is highly unpredictable and there are an infinite number of possible solutions, none of which teach or suggest the invention as claimed.

The Examiner has acknowledged (1) that the art of biotechnology is a highly unpredictable art, (2) that there is no prior art known to the Examiner that establishes that one of ordinary skill in the art would have known at the time the invention was made that all or any of the aldehyde compounds can be used as diagnosing marker for stroke/asymptomatic cerebral infarction, and (3) that the state of the art is that there is no art. Applicants respectfully urge that *KSR*'s focus in identified, predictable solutions may present a difficult hurdle in establishing obviousness in this highly unpredictable art because potential solutions are less likely to be genuinely predictable. See *Eisai v. Dr. Reddy's* (533 F3d, 1353, Fed. Cir. 2008).

Since at the time the invention was made, the claimed invention as a whole would not have been obvious to a person of ordinary skill in the art, Applicants respectfully urge that the Examiner withdraw this ground for rejection.

Double Patenting

Claims 1, 3, 4, and 6 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 2 of copending Application No. 12/598,125. The Examiner contended that although the conflicting claims are not identical, they are not patentably distinct from each other because they both claim detecting/diagnosing method of stroke/asymptomatic cerebral infarction by measuring aldehyde compound content.

Applicants' Response

Applicants have cancelled claims 1, 3, 4, and 6, rendering this rejection moot.

In view of the above remarks, it is respectfully submitted that the pending claims 9-24, are in condition for allowance and such action is earnestly solicited. If the Examiner believes that a telephone conversation would help advance the prosecution in this case, the Examiner is respectfully requested to call the undersigned at 973-360-7934. The undersigned also may be contacted via email at lubitb@gtlaw.

AUTHORIZATION

The Commissioner hereby is authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account 501561.

Respectfully submitted,
For Greenberg Traurig
By

Date: 12/16/10

Beverly W. Lubit, Ph.D.
Attorney for Applicant
Registration No. 47,759

Greenberg Traurig, LLP
200 Park Avenue
P.O. Box 677
Florham Park, NJ 07932
www.gtlaw.com